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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/596,876	11/28/2006	Daniel Tod Smithey	0003.0551/PC32026A	1776

152 7590 01/04/2011

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EXAMINER	
FUBARA, BLESSING M	

ART UNIT	PAPER NUMBER
1613	

MAIL DATE	DELIVERY MODE
01/04/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/596,876	SMITHEY ET AL.	
	Examiner	Art Unit	
	BLESSING M. FUBARA	1613	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 October 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45,46 and 49-62* is/are pending in the application.

4a) Of the above claim(s) *49-52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45,46 and 53-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The examiner acknowledges receipt of compliant amendment filed 10/14/20 and remarks filed 10/06/2010 and 10/14/2010. Claims 27-44, 47 and 48 are canceled. Claims 45 and 46 are amended. New claims 53-62 are added. Claims 45, 46 and 49-62 are pending and of these, claims 49-52 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 4/21/2010.

Response to Arguments

2. Previous rejections that are not reiterated herein are withdrawn. The rejection of claims 28, 30, 35-37, 39 and 40 under 35 U.S.C. 112, second paragraph, is withdrawn in view of the cancelation of these claims.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 28, 30, 35-37, 39 and 40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claims 55 and 56 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 55 recites that the mixture in claim 45, that is the mixture of drug, poloxamer and concentration enhancing polymer, is present in different regions of the composition; claim 56 recites that the mixture is present in different layers or multi-layer tablet. The limitations in claims 55 and 56 were not envisioned at the time the application was filed. Paragraph [0062] envisions: "The particles and concentration-enhancing polymer may be in different regions of the composition. For example, the particles may be in the form of a multi-layer tablet, as known in the art, wherein one or more layers comprises the amorphous drug and poloxamer and one or more different layers comprises the concentration-enhancing polymer. Yet another example may constitute a coated tablet wherein either the particles or the concentration-enhancing polymer or both may be present in the tablet core and the coating may comprise the concentration-enhancing polymer. Alternatively, the combination can be in the form of a simple dry physical mixture wherein both the particles and the concentration-enhancing polymer are mixed in particulate form and wherein the particles of each, regardless of size, retain the same individual physical properties that they exhibit in bulk." Thus it is the particle, that is, the drug and poloxamer, and the concentration enhancing polymer that are in different regions of the composition, the particle in the tablet core and the concentration enhancing polymer in the coating or vice versa; or the particles and the concentration enhancing polymer in different layers of multi-layer tablet.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 45, 46, 54 and 57-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Infeld et al. (WO 02/089835) in view of Beyerinck et al. (US 6,763,607).

10. Infeld discloses solid oral pharmaceutical dosage form of amorphous nelfinavir (abstract), which is in the form of powder or granules compressed into tablet (page 6, line 14; page 7, line 29; page 8, lines 14, 20-28). The dosage form comprising the nelfinavir, poloxamer and other excipients (see Examples IV and V) comprises greater than 50% of the particle by weight of the nelfinavir and poloxamer and this dosage form meets the limitation for at least 50% of particles of claim 45; the glass transition temperature of at least 50 °C as recited in claim 53 is a characteristic property of the drug and log P value of a drug that is greater than 6.5 as recited in claim 59 is the characteristic property of the drug. When the nelfinavir and poloxamer are

mixed at a temperature where the poloxamer is a solution ensures homogenous dispersion of the drug in the poloxamer in Infeld meets the homogeneous distribution of claim 54.

11. Claims 58-62 recite the properties of the dosage form such that these claims are met by the dosage of Infeld.

12. Infeld teaches that the nelfinavir is amorphous and as such the amorphous nature of the drug in claim 45 is met. The composition of Infeld in tablet form is intended for oral administration (page 4, lines 17, 31; page 5, line 2; page 17, lines 20, 21, 24).

13. One of the goals of Infeld is to make enhance the bioavailability and dissolution of nelfinavir (page 3, lines 16, 17; page 4, lines 25, 26).

14. The composition of Infeld does not contain concentration enhancing polymers. But it is known in the art that enhancing the concentration of poorly soluble drug also enhances the bioavailability of the poorly soluble drugs.

15. For example, Beyerinck discloses enhancing the concentration and bioavailability of a number of drugs, the work of Beyerinck is not limited to any specific drug except to the list of drugs disclosed in column 9, line 9 to column 11, line 19 and amongst this list is antivirals with acyclovir, nelfinavir and virazpole named antivirals (column 9, lines 11, 19, 20; column 10, line 16; column 11, lines 44, 45; column 12, lines 16-18; column 18, lines 61-64; column 19, lines 7, 17-19, 52-57; column 21, lines 54-59). Beyerinck also teaches that blends of polymers such as the enteric polymers and the copolymers of poyoxyethylenes and polyoxypropylenes, which are the poloxamers can be used in enhancing the concentration and bioavailability of poorly soluble drugs (see column 13, line 49, column 17, lines 16-45 and claim 20).

16. Neither Infeld nor Bayerinck teaches molecular dispersion.

17. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to enhance the bioavailability of the antiviral agent nelfinavir by using poloxamer. One having ordinary skill in the art would have been motivated to enhance the bioavailability and concentration of antivirals such as nelfinavir by using the teaching of Beyerinck where a blend of enteric polymers such as hydroxypropyl methyl cellulose acetate succinate, hydroxypropyl methyl cellulose phthalate, cellulose acetate phthalate, cellulose acetate trimellitate and poloxamer are used with the expectation of further enhancing the concentration and bioavaialability of nelfinavir.

18. Therefore, when the tablet formulation comprising a drug such as nelfinavir and poloxamer and enteric polymer such as hydroxypropyl methyl cellulose acetate succinate, hydroxypropyl methyl cellulose phthalate, cellulose acetate phthalate, cellulose acetate trimellitate, the composition of claims 45 and 46 are met and when the tablet comprising the drug, the poloxamer and the enteric polymer administered, then claim 57 is met since the composition after administration is in a use environment.

19. Claims 45, 46 and 54-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hoover et al. (US 20010053778 A1) and Babcock et al. (US 20010053791 A1).

20. Hoover is directed to pharmaceutical composition comprising glycogen phosphorylase (GPI), a sparingly soluble drug, in the form of amorphous solid dispersions and which is a simple physical mixture of the GPI and concentration enhancing polymer; the physical mixture in the case of oral administration constitutes layers where one or more of the layers comprise the amorphous GPI and one or more of the layers comprise the concentration enhancing polymer; Hoover also teaches that the GPI and the concentration enhancing polymer may be present in

different dosage forms (see paragraph [0193]); one of the goals of Hoover is to provide a composition comprising GPI and concentration enhancing polymer that improves the bioavailability of the GPI (see the whole document with emphasis on paragraphs [0011]-[0018], [0026], [0193]).

21. The composition of Hoover comprises various additives and excipients to promote the chemical and physical stability of the GPI (see paragraph [0207]). The composition of Hoover contains diluents such as lactose, mannitol, xylitol, microcrystalline cellulose, calcium diphosphate, and starch (paragraph [0200]). The dosage form of Hoover does not use poloxamer.

22. Babcock is also directed to physical mixture of glycogen phosphorylase inhibitor (GPI), concentration enhancing polymer, diluents such as lactose, mannitol, xylitol, dextrose, sucrose, sorbitol, compressible sugar, microcrystalline cellulose, powdered cellulose, starch, pregelatinized starch, dextrates, dextran, dextrin, dextrose, maltodextrin, calcium carbonate, dibasic calcium phosphate, tribasic calcium phosphate, calcium sulfate, magnesium carbonate, magnesium oxide, **poloxamers** such as polyethylene oxide, and hydroxypropyl methyl cellulose (paragraph [0126]); Babcock also teaches that the dosage form can be stabilized with additives such as various grades of polysorbate surfactant (paragraph [0142]) (see the whole document with emphasis on the title, paragraphs [0019], [0060], [0062], [0250], [0253]).

23. Thus, taking the teachings from Hoover and Babcock, one having ordinary skill in the art at the time the invention was made would be motivated to formulate GPI as layered tablet dosage form that contains concentration enhancing polymer, polysorbate for stabilizing the GPI, and diluents such as lactose, mannitol, xylitol, dextrose, sucrose, sorbitol, compressible sugar,

microcrystalline cellulose, powdered cellulose, starch, pregelatinized starch, dextrates, dextran, dextrin, dextrose, maltodextrin, calcium carbonate, dibasic calcium phosphate, tribasic calcium phosphate, calcium sulfate, magnesium carbonate, magnesium oxide, **poloxamers** such as polyethylene oxide, and hydroxypropyl methyl cellulose with the expectation that the bioavailability of the GPI is improved as anticipated by Hoover and Babcock.

24. When the physical mixture in the case of oral administration constitutes layers where one or more of the layers comprise the amorphous GPI and one or more of the layers comprise the concentration enhancing polymer the limitations of claims 54-56 are met. The drug composition comprising GPI, concentration enhancing polymer and poloxamer meets claims 45 and 46 since the GPI is amorphous and neither Hoover nor Babcock teaches molecular dispersion. Claims 58-62 recite the characteristic of the dosage form and thus, the modified dosage form of Hoover and Babcock meets the claims. The dosage form when administered would also have the physical mixture of GPI and concentration enhancing polymer and poloxamer in the same environment of use after administration.

25. No claim is allowed.

1. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BLESSING M. FUBARA whose telephone number is (571)272-0594. The examiner can normally be reached on Monday to Thursday from 7 a.m. to 5:30 p.m.

27. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brian Y. Kwon can be reached on (571) 272-0581. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

28. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Blessing M. Fubara/
Primary Examiner, Art Unit 1618